Closed Loop Stimulation in Vasovagal Syncope - One Year Follow-Up in Selected Patients

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Summary

Aim of the study was the evaluation of therapeutic effect of cardiac pacing on incidence of neurocardiogenic vasovagal syncope (NVS) during patient (pt) daily life. The recurrence of NVS and pt subjective health conditions before pacemaker (pm) implantation as well as during conventional and closed loop (CLS) DDD pacing were compared. Four pts, 2 male and 2 female, mean age 73.2 years (range 78 - 61), with an incidence of at least 2 NVS per year in the last 3-5 years and head-up tilt test (HUTT)-induced NVS for 2 consecutive times were included in the study. After implantation of INOS² CLS pm (Biotronik), pt was discharged in conventional DDD-mode for 3 weeks (w). At first follow-up, a HUTT was performed to provoke vasovagal reaction. Heart rate and arterial blood pressure were monitored. Pts were discharged in DDD-CLS pacing mode and HUTT was repeated after 2 w. Occurrence of NVS during HUTT disappeared in only 1/4 pt with conventional DDD pacing and in 3/4 pts with DDD-CLS pacing. Subjective quality of life after pm implant was good in all pts. No more NVS episodes were reported during daily life in one year follow up. Further investigations are necessary to understand in detail the preventive mechanisms shown by closed loop stimulation.

Key Words

Vasovagal syncope, closed loop stimulation, head-up tilt test

Introduction

The combination of an inappropriate slowing in cardiac rate, resulting from sudden augmentation of efferent vagal activity, and the hypotension caused by sudden reduction or cessation of the previously increased sympathetic outflow generates an abnormal and pathologic reflexed effect, which is known as Vasovagal syncope.

There are two different types of vasovagal syncope [1]:

1. The central or benign type, in which the medullary circulatory centers are directly affected by efferent hypothalamic signals triggered by emotional stress, pain, fear, etc.

2. The peripheral or malignant type, in which the central hypovolemia may be caused by impaired venoconstriction and a failure of normally increased tone of splenic and other resistance vessels [2].

In the second type of syncope, mechanoreceptors located within the ventricular myocardium are stimulated by the vigorous contraction of the insufficiently filled ventricle. Their afferent signal, conducted by the vagal nerve, reaches the circulatory centers triggering an increased efferent vagal activity and reducing the efferent sympathetic discharge [3,4]. The syncopal event is the expression of the severe hypotension and bradycardia resulting from this neuro-cardiac reflex [5]. The Head Up Tilt Test (HUTT) is the common clinic mean to provoke this peripheral type of vasovagal syncope. The sensibility of HUTT can be improved

with isoproterenol infusion to enhance the contractility response and to start the pathological reflex [6-8]. When the systolic pressure drops below the 50% of its basal value, without a decrease of the heart rate, there is a vasodepressive response. The response is defined "mixed" when a heart rate decrease (less than 60 bpm or asystolia) is associated to the decrease of systolic pressure (> 30%) [9].

At present, the pharmacological option for the prevention of the pathological reflex in vasodepressive syncope patients includes two opportunities. The first drug aims on decreasing myocardial contractility, while the second improves central volemia by peripheral vasoconstriction. DDI pacing can be additionally indicated besides drug therapy when there is a "mixed" response [10]. Dedicated algorithms in dual chamber pacing have been shown to improve prevention of syncopes: DDI with negative or positive hysteresis, DDI with rate drop response algorithm and DDD with automatic mode switching [11,12].

A new concept of cardiac pacing integrated into the natural cardiovascular control loop, the DDD Closed Loop Stimulation (CLS), seems to offer an important possibility to better prevent vasovagal malignant syncope with mixed response [13,14]. The integration of the device into the natural cardio-circulatory system is realized by monitoring the myocardial contractile dynamics, which reflect the information from the circulatory center even under pathophysiologic conditions. This concept ensures, that the heart rate is individually modulated according to the hemodynamic requirements. Since during vasovagal malignant syncope a change in contraction dynamics of the ventricular myocardium before and during the event occurs, a device based on CLS could be useful for its prevention. The CLS-principle is realized in the INOS^2 CLS (Biotronik GmbH, Germany) pulse generator by measuring the RV intracardiac impedance, which is determined by myocardial contractility variations. The loss of chronotropic competence is restored by the pacemaker, which becomes an integral part of the patient's physiologic circulatory regulation [15].

The aim of this study was to evaluate whether the INOS^2 CLS pacemaker provides pacing rates adequate to the patient's hemodynamic demand, especially during vasovagal syncope. The expected therapeutic effect should result in a marked decrease of syncopes during daily life and HUTT.

Methods

An INOS^2 CLS pulse generator was implanted in 4 patients (2 male, 2 female) mean age 73.2 years (range 78 - 61). Patients were selected according to the following criteria:

(a) 2 neurogenic vasovagal syncopes per year in the last 2-5 years,

(b) 2 consecutive HUTT (standard protocol) with a positive mixed response,

(c) no previous administration of drugs known to cause orthostatic hypotension;

(d) no positive response at right and left carotid sinus massage.

Patients were discharged with the pulse generator programmed in DDD-CLS mode.

At one month follow-up all patients were submitted to three consecutive HUTT (one per day) in a blind randomized stimulation mode: two tests in DDD (60 bpm lower rate) and one in DDD-CLS. The standard HUTT procedure was used with the patient in supine position for 10 minutes, then tilted-up to 70 degree for 45 minutes or until occurrence of the syncope.

The contractility response during HUTT in conventional DDD mode was registered by intracardiac impedance measurement using a special external device (Unilyzer, Biotronik), which was connected to the implanted device via telemetry. ECG was recorded continuously, while systolic and diastolic arterial blood pressures were measured every 2 minutes. Immediately after the onset of a syncope the HUTT was completed by lowering the patient to supine position. HUTT was repeated after 1-10 days with the same procedure.

In addition, the patients were asked to return to the clinic every three months to evaluate quality of life as well as the incidence of syncopal episodes during daily life possibly influenced by therapeutic effects of CLS pacing.

At six and twelve month follow-up, two HUTT were performed in DDD and DDD-CLS pacing mode.

Results

Table 1 presents the results of the 4 patients during preimplant and pacemaker follow-up.

One patient remained completely symptom free during HUTT after pm implant irrespectively of the pacing mode. In two patients, positive responses occurred in

Pt. (age, sex) Date of Imp.(m/y)	Pre-Imp. VVS episodes	Pre-Imp. HUTT	1 month HUTT			6m /1y HUTT		
			DDD	DDD-CLS	QoL	DDD	DDD-CLS	QoL
B. P. (76, m) 11/97	1995: 3 1996: 3 1997: 1	2 pos.	2 neg.	neg.	good, no more VVS	neg.	neg.	good, no more VVS
C.M. (75, f) 03/98	1997: 2 1998: 2	2 pos.	2 pos.	neg.	good, no more VVS	pos.	neg.	good, no more VVS
G. O. (78, f) 04/98	2/yr in last 5 ys	2 pos.	1. pos. 1 neg.	neg.	good, no more VVS	neg.	neg.	good, no more VVS
D.G. (61, m) 11/98	1998: 3	3. pos.	1 pos.	pos.	good, no more VVS	pos.	pos.	good, no more VVS

Notes. Date of implant m/y; VVS: Vasovagal Syncope; QoL: Quality of Life;

Table 1. Results of 4 patients during pre-implant and pacemaker follow-up.

DDD (once in one and twice in the other) but not in DDD CLS. All test were positive in the last patient, even in DDD-CLS pacing.

The evaluation of the intracardiac impedance, recorded by the Unilyzer device via telemetry, shows substantial differences with respect to syncope occurrence. Figures 1a and 1b depict the trends of the contractility parameter calculated from the intracardiac impedance in patient GO during two HUTTs in DDD mode at 1 month follow-up. Figure 1a shows the impedance trend during the positive HUTT: at the beginning of the test, when the patient reach the orthostatic position, there is an increase of contractility; which remains high up to the moment when the syncope occurs. At this time, contractility rapidly decreases and re-improves when the clinostatic position is reached by the patient. Figure

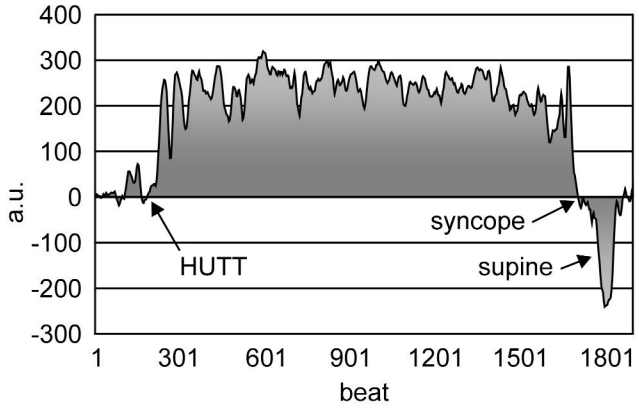

Figure 1a. Patient GO. Trend of intracardiac impedance during positive HUTT in DDD pacing at 1 month.

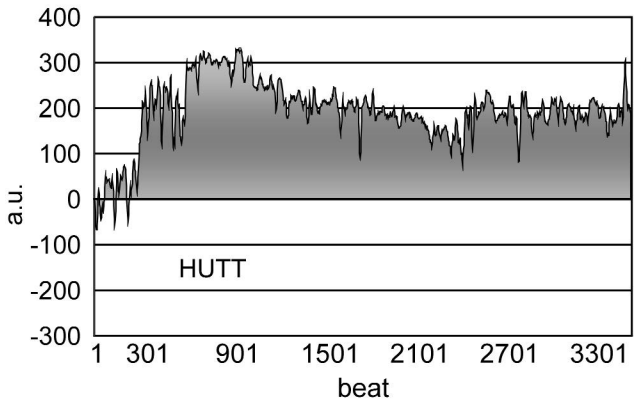

Figure 1b. Patient GO. Trend of intracardiac impedance during negative HUTT in DDD pacing at 1 month.

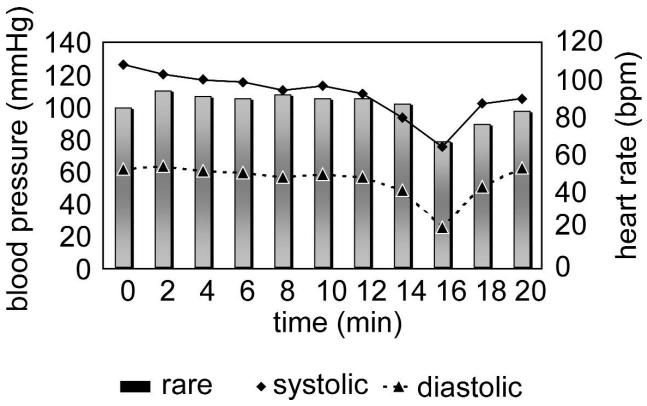

Figure 2. Patient CM. Trend of arterial blood pressures and heart rate during positive HUTT in DDD pacing.

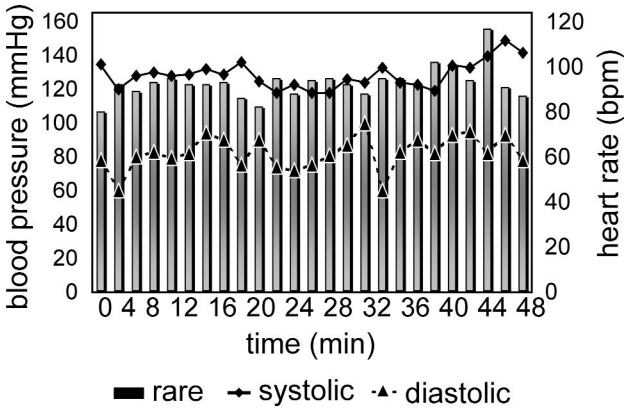

Figure 3. Patient CM. Trend of arterial blood pressures and heart rate during negative HUTT in DDD-CLS pacing.

1b shows the impedance trend during the negative HUTT: even in this case the contractility increases at the beginning of the test, but it stays high during the whole 45 minutes without any syncope.

Patient CM shows a mixed response during positive HUTT characterized by both a drop of arterial blood pressure and a decrease in heart rate (Figure 2).

When patient CM underwent the HUTT in DDD-CLS pacing, the increase of contractility induced an increase in the paced rate up to 110-120 bpm, which perhaps inhibited the hypotension reflex and the syncope (see Figure 3).

During the whole follow-up all patients reported a good quality of life and no more syncopal events during daily life.

Conclusion

Although our experience with DDD-CLS pacing mode is limited, this cardiac pacing concept promises to be effective in preventing the occurrence of vasovagal malignant syncope. Since the DDD-CLS pacing rate is increased according to contractility raise during both the first stage of HUTT and the presyncopal increase of the vagal tone, it prevents the failure of sympathetic tone and counterbalances the increase of vagal tone. Therefore, it limits arterial hypotension, heart bradycardia and, thus, avoids the occurrence of syncopal fainting. All 4 patients reported to be completely free of syncopes after pm implant, and their subjective health condition improved as well. Even the patient who suffered from syncopal events during all HUTTs, even in DDD-CLS mode, did not experience a syncope during daily life.

Similar promising results were achieved by other investigators using the INOS^2 CLS pulse generator to prevent vasovagal malignant syncope [16,17]. Moreover, comparable experiences are reported using a pulse generator with a different contractility sensor [18,19]. Nevertheless, some questions regarding the functionality of CLS are left open for further investigations:

- The change in contractility during the onset of a vasovagal reaction may be small in patients which generally show central hypovolumenia and increased vagal tone. A temporary system of contractility monitoring during preliminary HUTT to screen possibly unresponsiveness patient could be useful [20].
- It can be expected that the contractility response will be reduced by beta-blockers.
- The specificity of the CLS system to vasovagal reactions may be limited, since the system not only responds to pre-syncopal contractility variations but also to alterations of contractility from the more common and recurrent variations related to physiometabolic messages. It has to be investigated whether the resulting pacing rate can be partly elevated during patient daily life.

It can be concluded that these encouraging, but preliminary, results require further extensive studies to understand in detail the preventive mechanisms of closed loop stimulation in vasovagal malignant syncope and an extensive confirmation in a large population of patients.

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